








Osteoarthritis

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March 2021

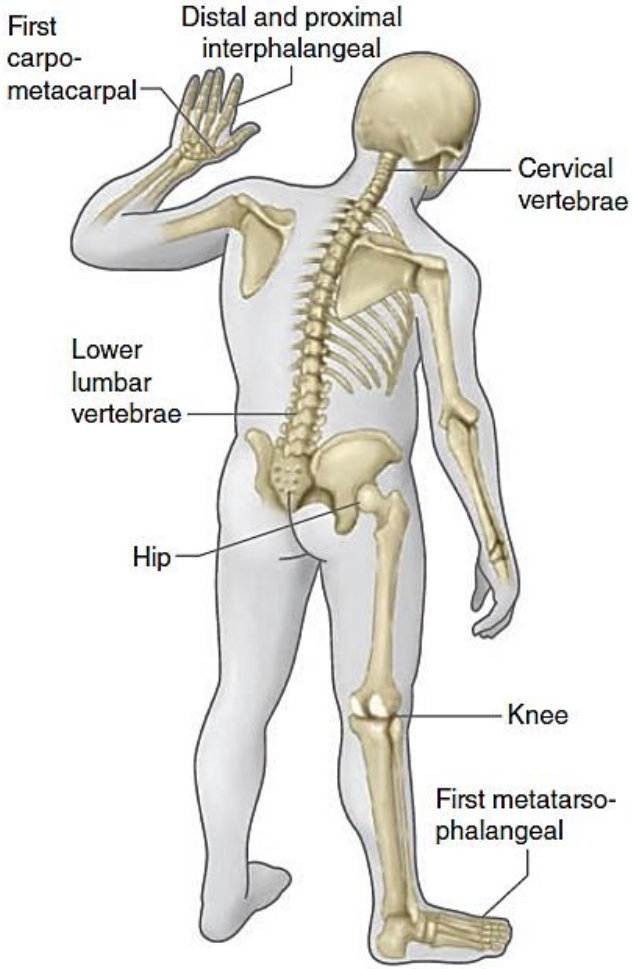
Definition

■ Chronic, progressive disorder characterized by the changes to articular cartilage and bone primarily in hands, knees, hips, and spine.

• Negative impact on physical function make it a leading cause of disability in the elderly.

Knee OA alone is as important a contributor to disability as cardiovascular disease and more important than other comorbidities.

→ Adversely affect quality of life.
& Imposes a tremendous **cost** burden.



Joints commonly affected by osteoarthritis

Epidemiology

- Depend on the definition used, such as symptomatic, radiographic, self-reported, or doctor-diagnosed;
It can be described pathologically, radiographically, or clinically.
… Prevalence and incidence rates vary across studies.

- **Not everyone with radiographic OA is symptomatic** :
Prevalence estimates for symptomatic OA tend to be **lower** than radiographic OA.

Prevalence

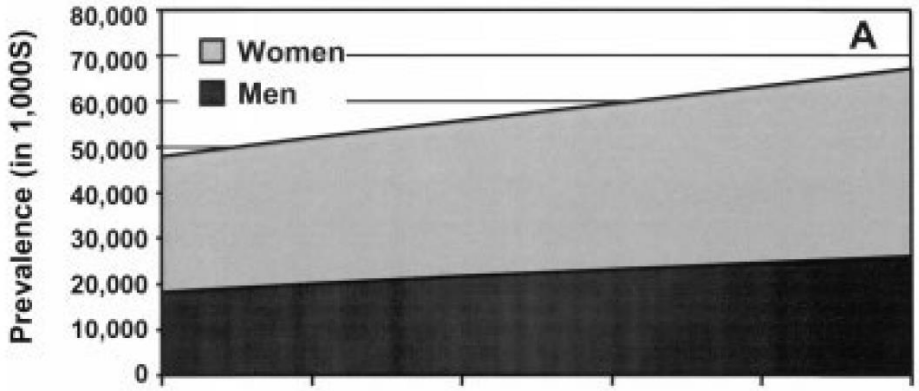
• During 2013 to 2015:
~ **54.4 million adults** in the US.
~ 23.7 million reporting AAAL.

• The prevalence of AAAL increased by almost 20% over time (2002-2015).

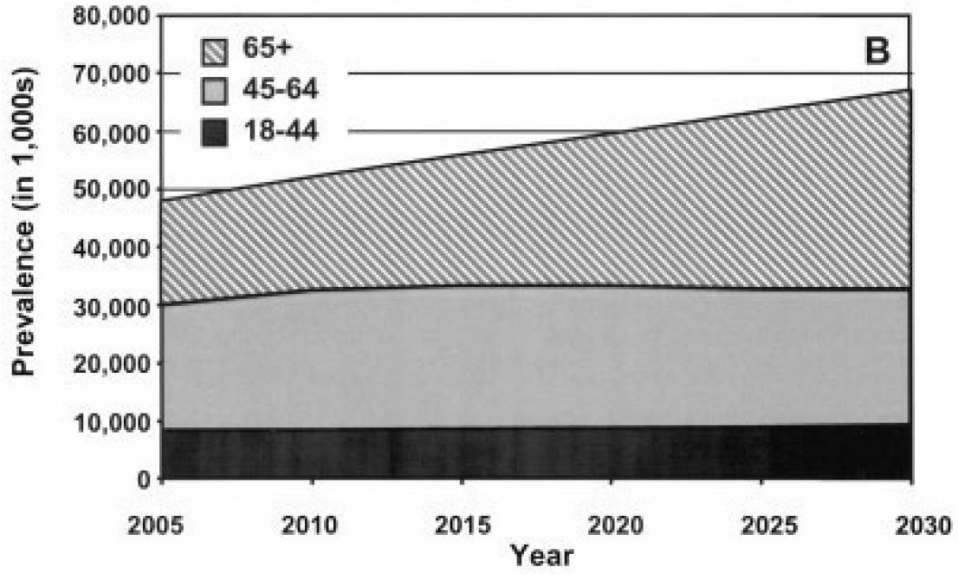
• Projected to affect **78.4 million adults** **by** **2040**.

• Increases with age, with just under 10 percent of men and 18 percent of women over the age of **60 years** reporting **symptomatic** OA.

ARTHRITIS & RHEUMATISM
Vol. 54, No. 1, January **2006**, pp 226–229
DOI 10.1002/art.21562



Projected prevalence of doctor-diagnosed arthritis in the US, 2005–2030, **by sex.**



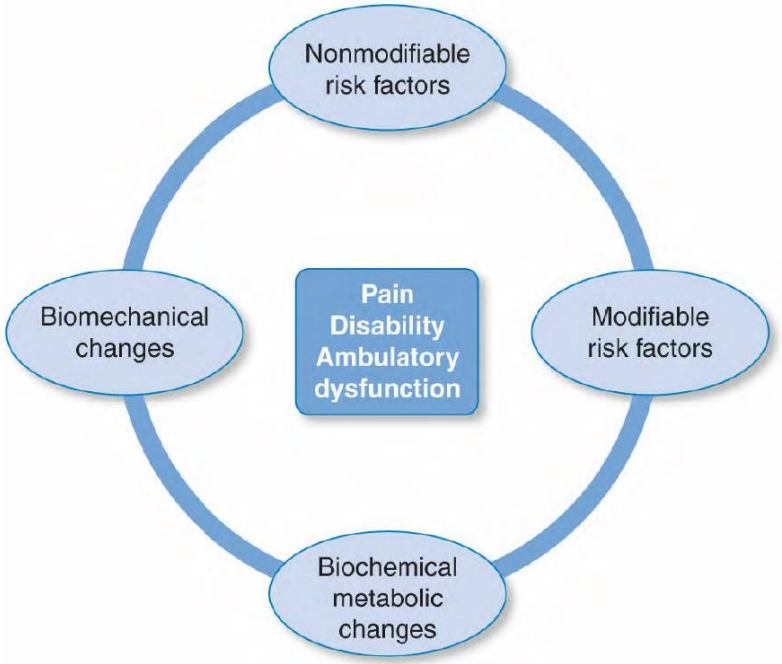
Projected prevalence of doctor-diagnosed arthritis in the US, 2005–2030, **by age**.

Etiology

- **Primary OA**:
cannot be traced to any particular identifiable cause.

- **Secondary OA**:
a known etiology or cause has been determined.

- Various risk factors:
  - Modifiable
  - Non-modifiable



Schematic representation of the convergence of modifiable, nonmodifiable risk factors, and morphologic changes associated with osteoarthritis.

Demographics

- Age
- Gender

Genetics

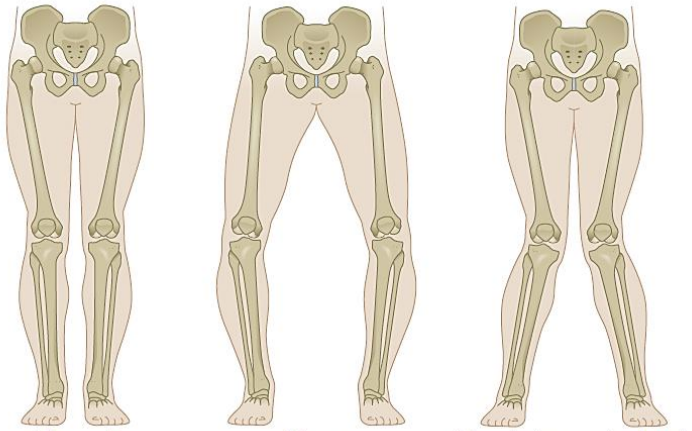
Joint injury

Lifestyle factors

- Obesity
- Occupation

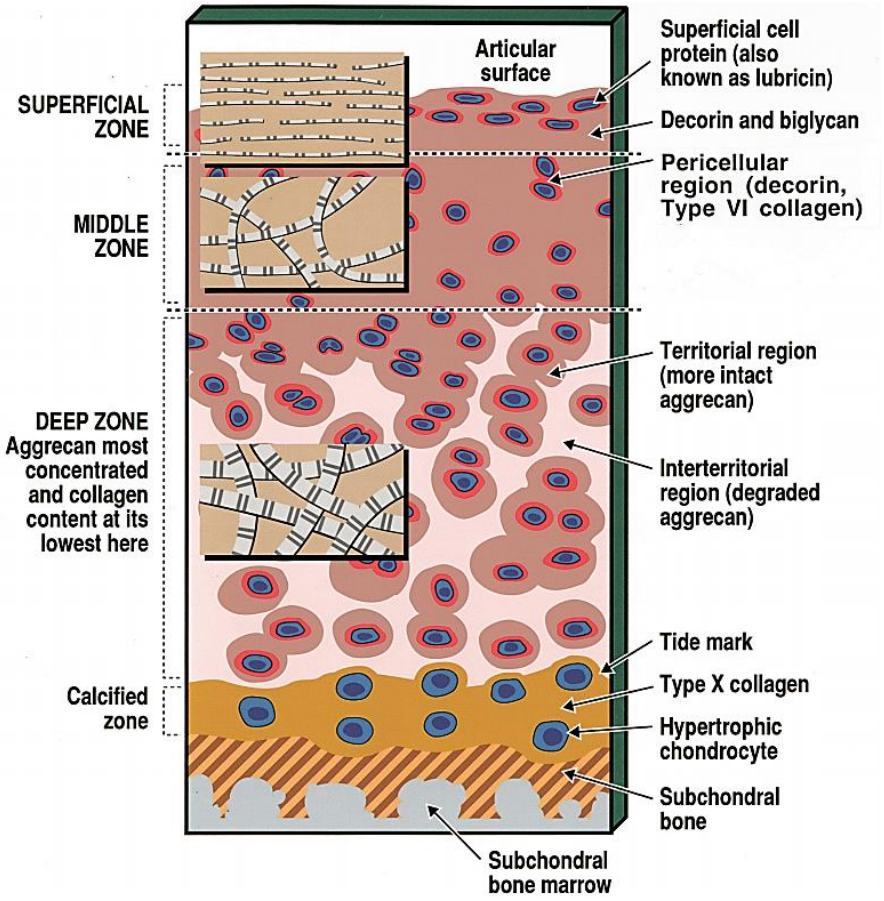
Other possible associations

- Muscle weakness/strength
- Smoking
- Bone density
- Physical activity



Anatomic factors

Pathogenesis



Healthy Joint

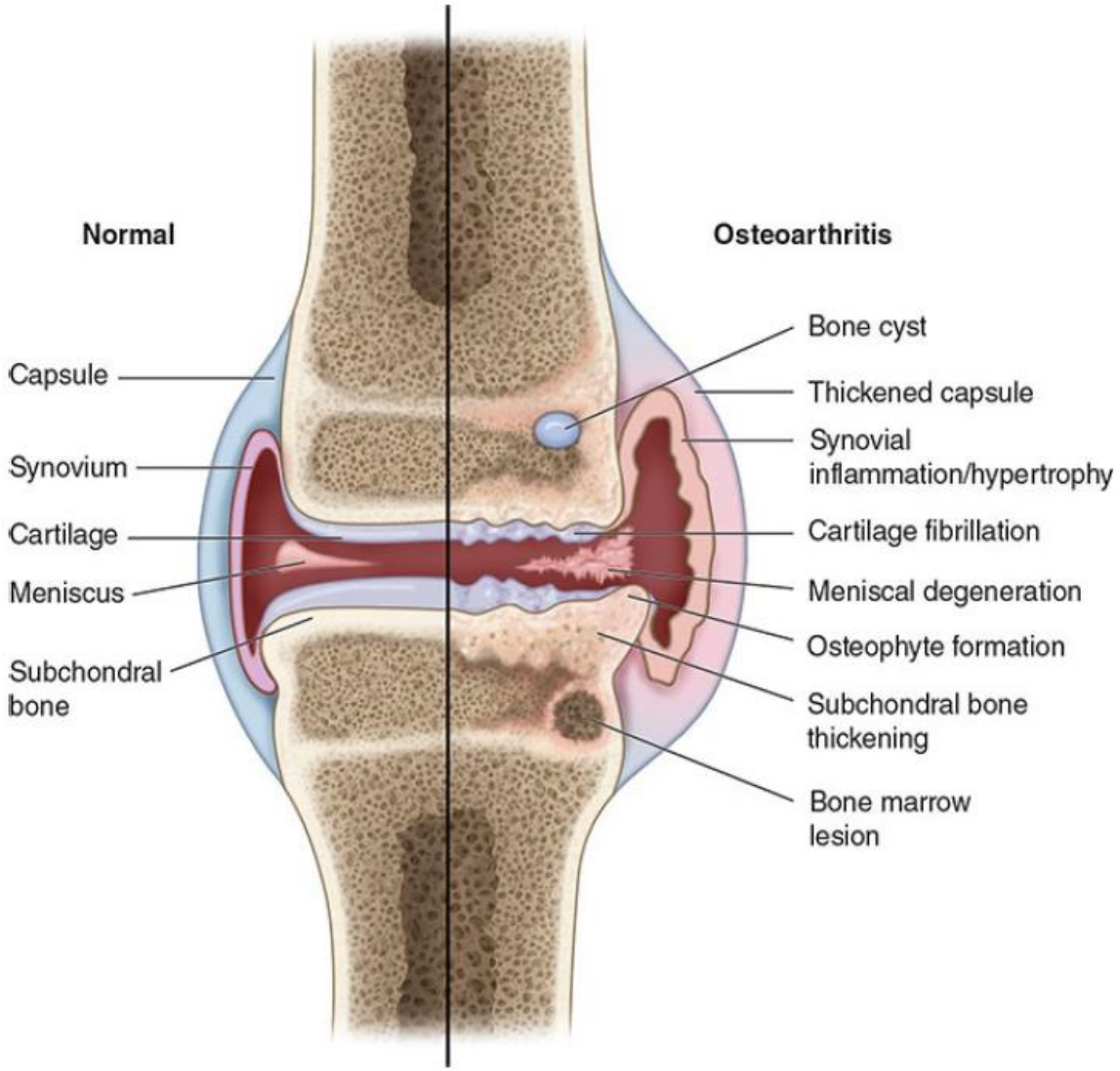
- Subchondral bone
- Cartilage
- Synovial
- Capsule
- Muscles

Normal Cartilage

The layer of cartilage is **narrow**:
Femoral articular cartilage:
Approximately 2 to 3 mm thick.

70% water,
10% collagen,
8% proteoglycans, chondrocytes, other proteins,
and long hyaluronic acid molecules.

Characteristics of osteoarthritis.



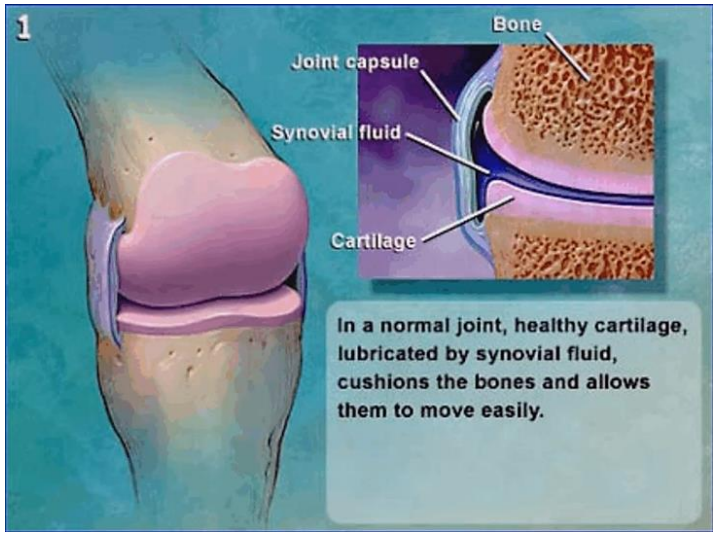
Cartilage remodeling

Synthesis activity

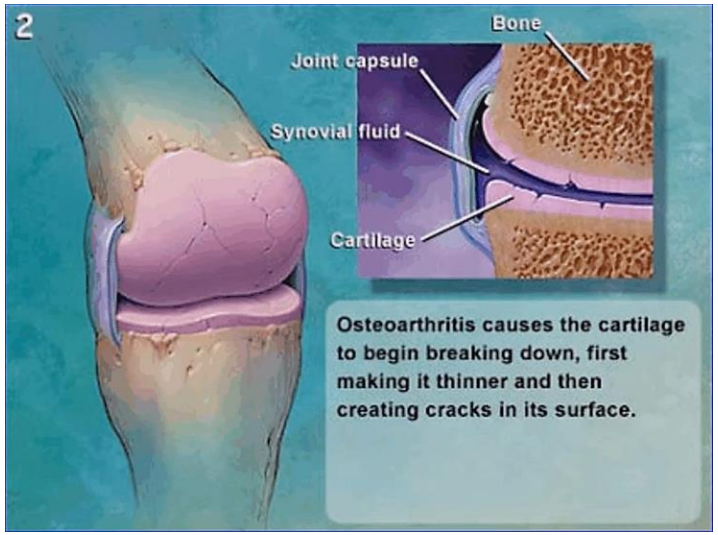
- Type II collagen
- Aggrecan

Degradative activity

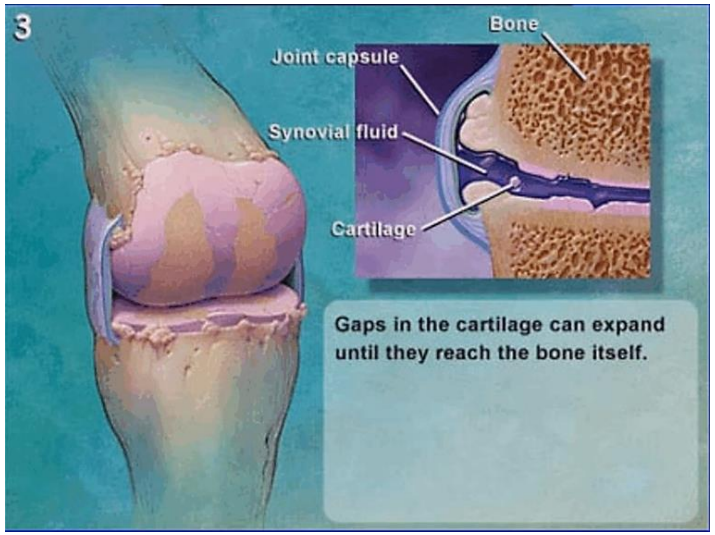
- TNF
- IL-1
- MMP
- NO



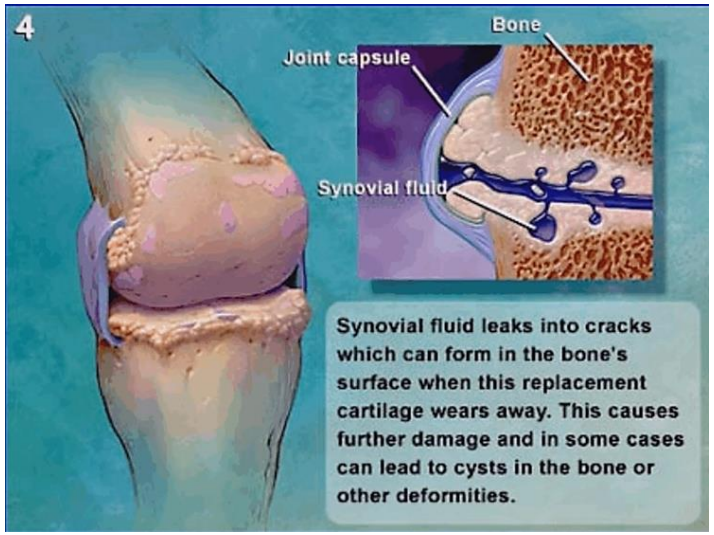
Normal Joint



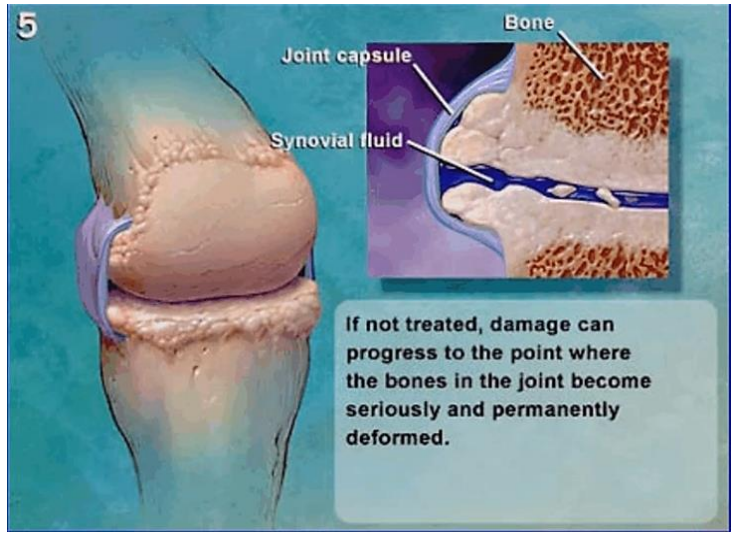
Cracking in cartilage



Gaps in cartilage



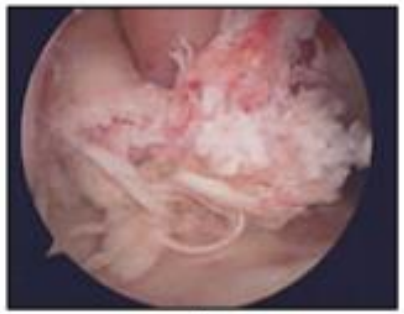
Gaps in Subchondral bone



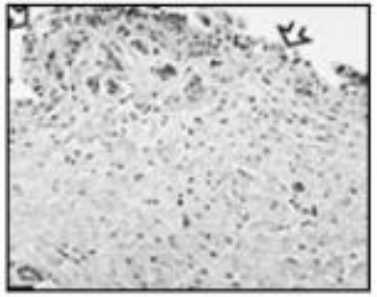
End stage OA

Meniscal damage

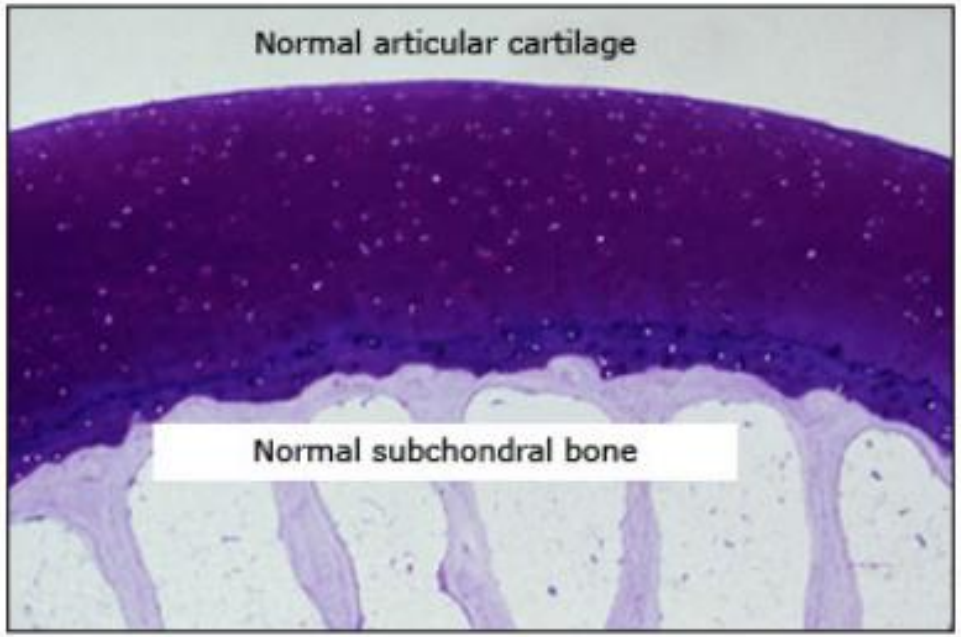
Ligament tears

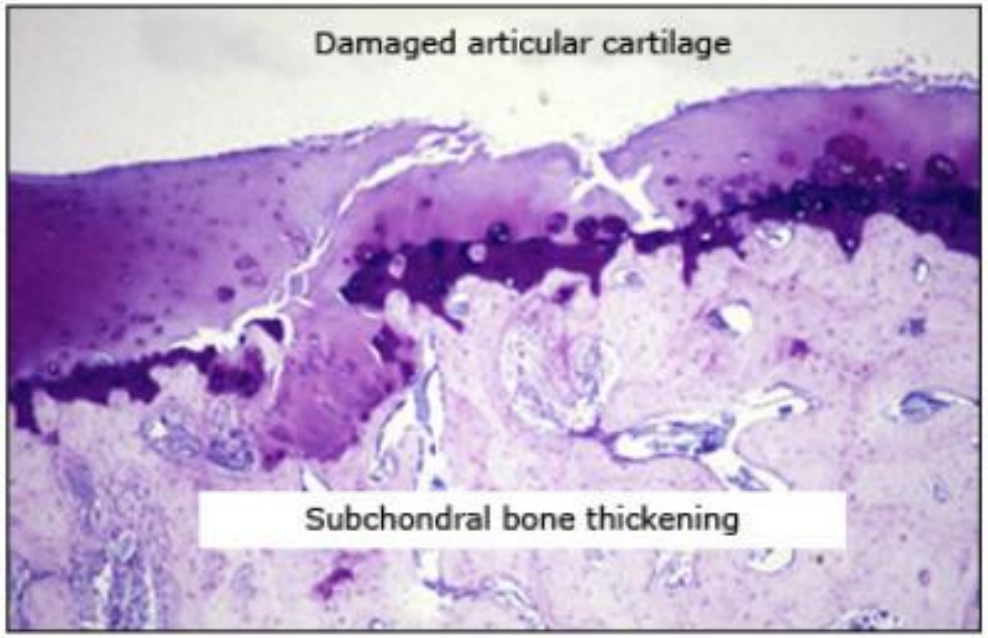


Synovitis



Cytokines, chemokines, growth factors, MMPs





Sources of pain

- Adult articular cartilage:

Aneural, cartilage loss in a joint is not accompanied by pain.
Avascular (Chondrocytes nourished by synovial fluid).
… **Pain in OA likely arises from structures outside the cartilage**.

- Synovial inflammation,
- Joint effusions,
- Bone marrow edema,
- Capsular stretching from fluid in the joint … stimulates nociceptive fibers…

Clinical Features

• Joint pain
(Either during or just after joint use and then gradually resolves)

Primarily **activity-related** in the early stages,
… As disease progresses, the pain becomes continuous.

- Stiffness of the affected joint,
but morning stiffness is usually brief (**<30 min**).

- Tenderness

- Limitation of motion

- Bony swelling

- Joint deformity

- Instability

Diagnosis

→ May be diagnosed without the use of radiography and/or laboratory investigations.

Clinical diagnosis :

May be diagnosed confidently on clinical grounds alone if the following are present:

- **Persistent usage-related joint pain in one or few joints**
- **Age ≥ 45 years**
- **Morning stiffness ≤30 minutes**

Principal manifestations of osteoarthritis

Patient characteristics	
Age of onset	> 40 years
Symptoms	
Pain	• Affects one or a few joints at a time • Insidious onset - slow progression over years • Variable intensity • May be intermittent • Increased by joint use and relieved by rest • Night pain in severe osteoarthritis
Stiffness	Short-lived (<30 minutes) and early morning- or inactivity-related
Swelling	Some (eg, nodal osteoarthritis) patients present with swelling and/or deformity
Constitutional symptoms	Absent
Physical exam findings	
Appearance	• Swelling (bony overgrowth ± fluid/synovial hypertrophy) • Deformity • Muscle wasting (global - all muscles acting over the joint)
Palpation	• Absence of warmth • Swelling (effusion if present is usually small and cool) • Joint line tenderness • Periarticular tenderness (especially knee, hip)
Range of motion	• Crepitus (knee, thumb bases) • Reduced range of movement • Weak local muscles

When to consider additional testing ?

Appropriate imaging and laboratory investigations should be carried out in:

- Younger individuals with joint symptoms/signs of OA

- Presence of **atypical** symptoms and signs such as an unusual site of involvement, symptoms and signs of joint inflammation, marked rest and/or night pain, and rapidly progressive pain.

- Presence of weight loss or constitutional symptoms

- Those with knee pain and true "locking," which suggests additional mechanical derangement

ESR
CRP
RF
....

- Radiographic examination …
- Synovial fluid examination is not routinely required …

Treatment

(1) To **educate** the patient, family members, and caregivers;
(2) To relieve pain and **stiffness**;
(3) To maintain or improve joint **mobility**;
(4) To limit functional **impairment**;
(5) To maintain or improve **quality of life**.

Arthritis Care & Research
Vol. 72, No. 2, February 2020, pp 149–162
DOI 10.1002/acr.24131

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee

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Nonpharmacologic Therapy

- Patient education
- Exercise
- Weight loss (if overweight)
- Use of assistive device (ie. Cane)
- Use of shoe insoles
- Application of heat
- Use of fitted knee braces
- Passive exercise alone

.....

PHYSICAL, PSYCHOSOCIAL, and MIND-BODY APPROACHES

HAND	KNEE	HIP
	Exercise*	
	Self-Efficacy and Self-Management Programs	
	Weight Loss	
	Tai Chi	
	Cane	
1st CMC Orthosis	TF Knee Brace**	
	Heat, Therapeutic Cooling	
	Cognitive Behavioral Therapy	
	Acupuncture	
	Kinesiotaping	
	Balance Training	
Other Hand Orthoses***	PF Knee Brace**	
Paraffin	Yoga	
	RFA	

HAND	KNEE	HIP
	TENS	
Iontophoresis	Manual Therapy (with or without exercise)	
	Massage Therapy	
	Modified Shoes	
	Wedged Insoles	
	Pulsed Vibration Therapy	

Strongly recommended

Conditionally recommended

Strongly Against

Conditionally Against

PHYSICAL, PSYCHOSOCIAL, and MIND-BODY APPROACHES

Intervention	Joint		
	Hand	Knee	Hip
Exercise			
Balance training			
Weight loss			
Self-efficacy and self-management programs			
Tai chi			
Yoga			
Cognitive behavioral therapy			
Cane			
Tibiofemoral knee braces		(Tibiofemoral)	
Patellofemoral braces		(Patellofemoral)	
Kinesiotaping	(First carpometacarpal)		
Hand orthosis	(First carpometacarpal)		
Hand orthosis	(Other joints)		
Modified shoes			
Lateral and medial wedged insoles			
Acupuncture			
Thermal interventions			
Paraffin			
Radiofrequency ablation			
Massage therapy			
Manual therapy with/without exercise			
Iontophoresis	(First carpometacarpal)		
Pulsed vibration therapy			
Transcutaneous electrical nerve stimulation			

Strongly recommended
Conditionally recommended
Strongly recommended against
Conditionally recommended against
No recommendation

Pharmacologic Therapy

- Available drugs are administered using oral, topical, and intraarticular routes.
- To date, there are no available drugs that alter the disease process itself.

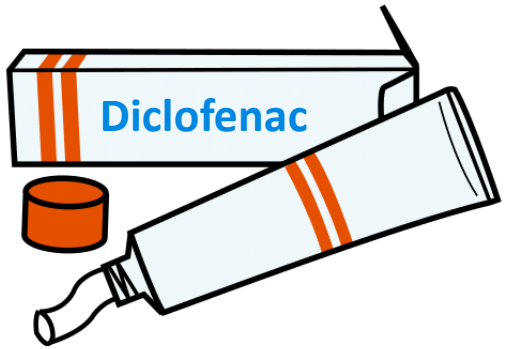
Acetaminophen

- The first choice for the treatment of mild-to-moderate OA.
- Differ in their **strength of recommendation**, **dosing**, and **length of therapy**.
- Can be taken at 325 to 650 mg every 4 to 6 hours (must not exceed 4 g daily).
- **Hepatotoxicity**

Topical NSAIDs

- As a potential first-line therapy for joint-specific OA.
- Should be considered prior to use of oral NSAIDs.
- Slightly less efficacious than oral agents,
- But have far fewer GI and systemic side effects.

Often cause local skin irritation where the medication is applied :
Redness,
Burning,
Itching.



Oral NSAIDs

- The most popular drugs to treat osteoarthritic pain.
- **Strongly recommended** (regardless of anatomic location).
- Produce **~30%** greater improvement in pain than high-dose acetaminophen.
- Initially, "as needed"
- Doses : as low as possible,
- Duration: as short as possible.

Side effects:

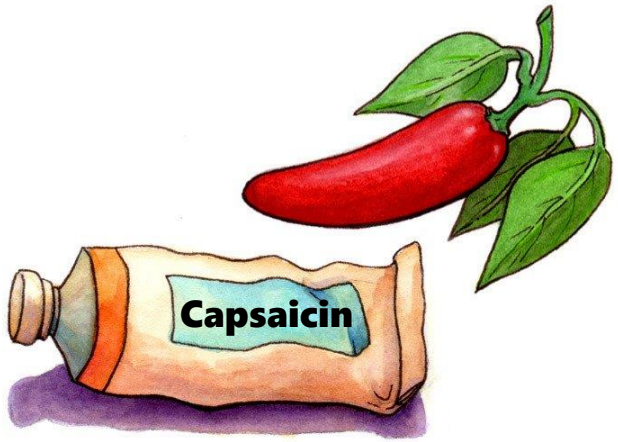
- Gastrointestinal Effects
- Cardiovascular Risk
- Drug-induced hepatitis
- Renal toxicity
- Other toxicity……

Capsaicin

- Isolated from hot peppers,
- Releases and ultimately depletes substance P from afferent nociceptive nerve fibers.

Adverse Effects :
- Primarily local including burning, stinging, and/or erythema ,
That usually subsides with repeated application.
- Systemic effects are rare. (Coughing associated with application).

Dosing and Administration :
To be effective, must be used **regularly**,
May take up to **2 weeks** to take effect,
Recommended **4 times a day**.



Intra-articular Corticosteroids

Triamcinolone acetonide
Methylprednisolone acetate

✘ **Adverse Events** :
Can be local or systemic in nature.
Systemic : hyperglycemia, edema, elevated blood pressure, flushing, dyspepsia and hypercortisolism.
Local : infection in the affected joint, osteonecrosis, tendon rupture, and skin atrophy at the injection site.

Systemic corticosteroid therapy is not recommended in OA,
given the lack of proven benefit and the well-known adverse effects with long-term use.

Dosing and Administration :

• Average doses for injection of large joints in adults :
40 mg of triamcinolone and methylprednisolone acetate.

• Local anesthetics such as lidocaine or bupivacaine : to provide rapid pain relief.

• Generally limited to **3 or 4 injections per year** due to the potential systemic effects of corticosteroids and because the need for more frequent injections indicates little response to the therapy.

After injection, ……The patient should minimize activity and stress on the joint for several days.

- Initial pain relief : May be seen **within 24 to 72 hours** after injection,
- Peak pain relief : **About 7 to 10 days** after injection,
- Lasting : Up to **4 to 8 weeks**.

Tramadol

- Affinity for the μ-opioid receptor,
- Weak inhibition of the reuptake of norepinephrine and serotonin neurotransmitter.

✘ **Adverse Events & Interaction** :

Opioid-like adverse effects …

The most notable serious adverse event : **Seizures**

…. Medications that lower the seizure threshold should be used with caution.

Increased risk of **serotonin syndrome**.

Dosing and Administration :

- Should be initiated at a lower dose (100 mg/day),
- May be titrated as needed for pain control to a dose of 200 mg/day,
- With a maximum dose of 400 mg/day.
- Requires dose adjustment with diminished renal function.

Duloxetine

- Approved for the treatment of chronic musculoskeletal pain.
- Increases the risk of serotonin syndrome.

✘ **Adverse effects** :
Nausea,
Dry mouth,
Constipation,
Anorexia.
Expected neurologic adverse effects :
Fatigue,
Somnolence,
Dizziness

Serious adverse events :
Stevens-Johnson syndrome
Liver failure

Hyaluronic Acid Injections

Exogenous intra-articular hyaluronate is available as a treatment for the symptoms of knee OA :

- Provide and maintain intra-articular lubrication,
- Anti-inflammatory,
- Analgesic,
- Chondroprotective effects.

Evidence has **not** shown intra-articular HA to have a clinically significant benefit.

✘ **Adverse effects :**

- Acute joint swelling,
- Effusion,
- Stiffness,
- Rash,
- Ecchymoses,
- Pruritus.

Rarely :

- Hypersensitivity reactions
- Joint infections

Dosing and Administration :

• Most HA products are injected once **weekly** for **either 3 or 5 weeks**, depending on the specific agent administered.

• Patients are generally advised to repeat the injection schedule **by 6 months** **if** they are satisfied with the previous course.

• Strenuous or prolonged weight-bearing activities **should be avoided for 48 hours** after treatment.

• Routinely, the most improvement is expected :
From **5 to 13 weeks** after injection with some effect still occurring at 24 weeks.

Glucosamine and Chondroitin

- Ability to stimulate proteoglycan synthesis from articular cartilage in vitro.

The American College of Rheumatology

- **Glucosamine** is **strongly recommended against** in patients with knee, hip, and/or hand OA.
- **Chondroitin** sulfate is **strongly recommended against** in patients with knee and/or hip OA as are **combination** products that include glucosamine and chondroitin sulfate, but is **conditionally recommended for patients with hand OA.**

PHARMACOLOGIC APPROACHES

HAND	KNEE	HIP
Oral NSAIDs		
Topical NSAIDs	Topical NSAIDs	
I-A Steroids	I-A Steroids (Imaging-Guidance for Hip)	
Acetaminophen		
Tramadol		
Duloxetine		
Chondroitin	Topical Capsaicin	

HAND	KNEE	HIP
Bisphosphonates		
Glucosamine		
Hydroxychloroquine		
Methotrexate		
TNF Inhibitors		
IL-1 Receptor Antagonists		
	PRP	
	Stem Cell Injection	
Chondroitin	Chondroitin	
Intra-Articular Hyaluronic Acid		I-A Hyaluronic Acid
	Intra-Articular Botulinum Toxin	
Topical Capsaicin	Prolotherapy	
Colchicine		
Non-Tramadol Opioids		
Fish Oil		
Vitamin D		

Strongly recommended

Conditionally recommended

Strongly Against

Conditionally Against

PHARMACOLOGIC APPROACHES

Intervention	Joint		
	Hand	Knee	Hip
Topical nonsteroidal antiinflammatory drugs			
Topical capsaicin			
Oral nonsteroidal antiinflammatory drugs			
Intraarticular glucocorticoid injection			
Ultrasound-guided intraarticular glucocorticoid injection			
Intraarticular glucocorticoid injection compared to other injections			
Acetaminophen			
Duloxetine			
Tramadol			
Non-tramadol opioids			
Colchicine			
Fish oil			
Vitamin D			
Bisphosphonates			
Glucosamine			
Chondroitin sulfate			
Hydroxychloroquine			
Methotrexate			
Intraarticular hyaluronic acid injection	(First carpometacarpal)		
Intraarticular botulinum toxin			
Prolotherapy			
Platelet-rich plasma			
Stem cell injection			
Biologics (tumor necrosis factor inhibitors, interleukin-1 receptor antagonists)			

Strongly recommended
Conditionally recommended
Strongly recommended against
Conditionally recommended against
No recommendation

WOMAC Survey Form Name: _____

Instructions: In Sections A, B, and C, questions will be asked about your hip or knee pain. Please mark each response with an X. If you are unsure about how to answer a question, please give the best answer you can.

A. Think about the pain you felt in your hip/knee during the last 48 hours.

Question: How much pain do you have?	None	Mild	Moderate	Severe	Extreme
1. Walking on a flat surface	☐	☐	☐	☐	☐
2. Going up and down stairs	☐	☐	☐	☐	☐
3. At night while in bed, pain disturbs your sleep	☐	☐	☐	☐	☐
4. Sitting or lying	☐	☐	☐	☐	☐
5. Standing upright	☐	☐	☐	☐	☐

B. Think about the stiffness (not pain) you have in your hip/knee during the last 48 hours. Stiffness is a sensation of decreased ease in moving your joint.

	None	Mild	Moderate	Severe	Extreme
6. How severe is your stiffness after first awakening in the morning?	☐	☐	☐	☐	☐
7. How severe is your stiffness after sitting, lying, or resting in the day?	☐	☐	☐	☐	☐

C. Think about the difficulty you had in doing the following daily physical activities due to your hip/knee during the last 48 hours. By this we mean your ability to move around and look after yourself.

Question: What degree of difficulty do you have?	None	Mild	Moderate	Severe	Extreme
8. Descending stairs	☐	☐	☐	☐	☐
9. Ascending stairs	☐	☐	☐	☐	☐
10. Rising from sitting	☐	☐	☐	☐	☐
11. Standing	☐	☐	☐	☐	☐
12. Bending to the floor	☐	☐	☐	☐	☐
13. Walking on flat surfaces	☐	☐	☐	☐	☐
14. Getting in and out of a car, or on or off a bus	☐	☐	☐	☐	☐
15. Going shopping	☐	☐	☐	☐	☐
16. Putting on your socks or stockings	☐	☐	☐	☐	☐
17. Rising from the bed	☐	☐	☐	☐	☐
18. Taking off your socks or stockings	☐	☐	☐	☐	☐
19. Lying in bed	☐	☐	☐	☐	☐
20. Getting in or out of the bath	☐	☐	☐	☐	☐
21. Sitting	☐	☐	☐	☐	☐
22. Getting on or off the toilet	☐	☐	☐	☐	☐
23. Performance heavy domestic duties	☐	☐	☐	☐	☐
24. Performing light domestic duties	☐	☐	☐	☐	☐

HSS ☐☐ - ☐☐ - ☐☐

Draft

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Other Dietary Supplements

Methyl sulfonyl methane (MSM)

- In some green plants, fruits, and vegetables.
- Anti-inflammatory & analgesic effects.

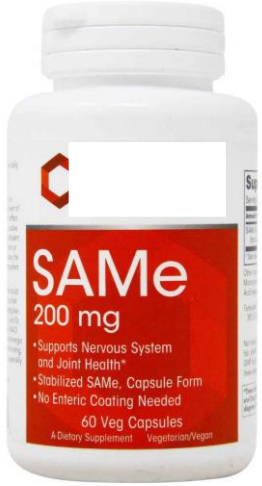
… Need to be investigated in large clinical trials.

S-adenosyl methionine (SAMe)

- Produced in the liver from methionine.
- Anti-inflammation & direct analgesic effects,

(Potentially mediated through inhibition of COX).

… Need to be investigated in large clinical trials.



Avocado soybean unsaponifiables (ASUs)

- Made up of fractions of one-third avocado oil and two-third soybean oil.
- Chondroprotective, anabolic, & anti-inflammatory effects.

… Appear to be beneficial for modestly improving OA Symptoms, but slows the **structural progression of OA** needs to be investigated in larger randomized controlled trials.

Harpagophytum procumbens (Devil's Claw)

- African plant that gets its name from the "claws" found on the fruit.
- Anti-inflammatory effects, possibly due to inhibition of COX and lipoxygenase.

…. More evidence from high-quality clinical trials is needed

Turmeric (Curcuma longa)

- A yellow spice
- Anti-inflammatory effects due to inhibition of COX-2, prostaglandins, and leukotrienes.

… More rigorous and larger trials are needed.

Zingiber officinale (Ginger)

- Anti-inflammatory effects by inhibiting COX and lipoxygenase & decrease the synthesis of inflammatory prostaglandins.

… there is not enough evidence to support recommending ginger.

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Thank You
For Your Kind Attention